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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/661,927	09/14/2000	William J. Dower	019282-000110US	1158
20350 7590 11/16/2007 TOWNSEND AND TOWNSEND AND CREW, LLP TWO EMBARCADERO CENTER EIGHTH FLOOR SAN FRANCISCO, CA 94111-3834			EXAMINER EPPERSON, JON D	
			ART UNIT 1639	PAPER NUMBER
			MAIL DATE 11/16/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

09/661,927

Applicant(s)

DOWER ET AL.

Examiner

Jon D. Epperson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 August 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-70,72,75-77 and 138-142 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 69,70,72,76,77 and 142 is/are allowed.
- 6) ☒ Claim(s) 1,3-68,75 and 138-141 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 12/1/03.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- ☐ Notice of Informal Patent Application
- ☐ Other: _____.

DETAILED ACTION

Status of the Application

1. The Response filed August 20, 2007 is acknowledged.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior office action.

Status of the Claims

3. Claims 1, 3-77, 138 and 139 were pending. Applicants amended claims 1, 4, 6, 12, 14, 19-20, 22-24, 26, 41, 46, 48, 49, 51, 52, 56, 65, 68-70, 72, 75-77, and 138. In addition, claims 140-142 were added and claims 71, 73, and 74 were canceled. Therefore, claims 1, 3-70, 72, 75-77, and 138-142 are currently pending and examined on the merits. Please note that the restriction requirement with regard to Groups I-III as set forth in the 4/1/03 Restriction requirement is hereby withdrawn (i.e., Groups I-III are considered to be one Group), which is consistent with Applicants' current claims drawn to the screening of both the "protein and/or a ligand/substrate thereto" (e.g., see claim 140). Please note that once a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Withdrawn Objections/Rejections

4. The objection to claim 64 is withdrawn in view of Applicants' arguments (e.g., see 8/20/07 Response, section 3A). The rejections denoted "A" (in part) and "C-G" under 35 U.S.C.

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§ 112, second paragraph are withdrawn in view of Applicants' amendments to claims 1, 4, 6, 12, 14, 19, 20, 22, 56, 69, 70, 72, 75-77 and arguments in sections 4 A and C-G. The Homolya et al. rejection under 35 U.S.C. § 102 is withdrawn in view of Applicants' amendments to claim 69. It is noted that the "AM" portions of fluorophores like BCECF-AM, Fura-2, Quin-2, etc. (e.g., see Homolya et al., figure 2) do not fall within the scope of the compound/fluorophore/quencher moiety because the fluorophore must be linked to the quencher via a linker (e.g., see independent claims 1 and 69), which is not the case for these molecules. That is, the potential "quencher" (i.e., the AM portion of each molecule) is attached directly to the fluorophore without the use of a linker. Furthermore, even if, *assuming arguendo*, the "first part" of the AM that is directly attached to the fluorophore (e.g., the cleavable ester) could be considered a linker; this part would still play a role as a quencher (e.g., blocking the ability of a heteroatom to donate electrons to a ring system) and thus would still need to be attached to the fluorophore via "another linker" that does not quench the fluorophore because, as mentioned above, a quencher cannot be directly attached to the fluorophore (including a quencher that also acts as a linker). This is consistent with Applicants' specification that provides examples like acylated coumarins that function as "quenched" fluorophores (e.g., see page 35, lines 21-25). These acylated coumarins fall outside the scope of the current claims, just as the "AM" compounds do, because they do not possess anything (i.e., a linker) between the quencher and the fluorophore. The atoms that are directly attached to the fluorophore also play a role in "quenching" the molecule. The Swanson et al. reference is withdrawn (in part) under 35 U.S.C. § 102 for the same reasons as set forth above for Homolya et al. All other rejections are maintained and the arguments are addressed below.

Outstanding Objections and/or Rejections

Claim Rejections - 35 USC § 112, second paragraph

5. Claim 1, 3-68, 138 and 139 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. For ***claim 68*** use of the word “type” in the phrase “carrier-type” is vague and indefinite. The addition of the word “type” to an otherwise definite expression extends the scope of the expression so as to render it indefinite. See Ex parte Copenhaver, 109 USPQ 118 (Bd. App. 1955). See also MPEP § 2173.05(b). Therefore, claims 68 and all dependent claims are rejected under 35 U.S.C. § 112, second paragraph.

B. ***Claim 1*** recites the limitation "the plasma membrane of a cell surface" in line 2. There is insufficient antecedent basis for this limitation in the claim. Therefore, claim 1 and all dependent claims are rejected under 35 USC 112, second paragraph.

C. Withdrawn.

D. Withdrawn.

E. Withdrawn.

F. withdrawn.

G. Withdrawn.

Response

6. Applicant's arguments directed to the above 35 U.S.C. 112, second paragraph rejections

were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection might have been modified from its original version to more clearly address applicants' newly amended and/or added claims and/or newly amended arguments.

A. Applicants argued that they had removed all the "carrier-type" language from the claims including claim 68 (e.g., see 8/20/07 Response, section 41; see also partial amendment to claim 68).

This is not found persuasive for the following reasons:

The "carrier-type" language still exists in claim 68 (i.e., Applicants removed the language from step (b) of claim 68 but not step (a)).

B. Applicants argue that they have amended the claims to obviate the rejection (e.g., see 8/20/07 Response, section 4b).

This is not found persuasive for the following reasons:

The Examiner respectfully disagrees. Step (b) does not provide antecedent basis for the preamble because it occurs after the preamble. Furthermore, not all cell surfaces contain a plasma membrane. Thus, "the plasma membrane" in line 2 was not properly introduced.

Accordingly, the 35 U.S.C. 112, second paragraph rejections cited above are hereby maintained.

Claims Rejections - 35 U.S.C. 102

7. Claim 75 is rejected under 35 U.S.C. 102(b) as being anticipated by Swanson et al.

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(Swanson, S. J.; Bethke, P.; Jones, R. L. "Barley Aleurone Cells Contain Two Types of Vacuoles: Characterization of Lytic Organelles by Use of Fluorescent Probes" *The Plant Cell* **May 1998**, *10*, 685-698) (of record) as evidenced by Ozkan et al. (Ozkan P.; Mutharasan, R. "A rapid method for measuring intracellular pH using BCECF-AM" *Biochim. Biophys. Acta.* **2002**, *1572*, 143-148) (of record).

For **claim 75**, Swanson et al. disclose a method of screening for a carrier mediated transport protein and/or a ligand thereto comprising (a) providing a library comprising different complexes, each complex comprising a compound and a separate reporter, the compound varying between different complexes (e.g., see figure 4 wherein the different compounds are the CH₂Cl and CH₂SG and the reporter is the 2H-chromen-2-one ring or, alternatively, the ring attached to ZFR or some portion thereof). Swanson et al. also disclose (b) providing a plurality of different cells that are located within a single reaction vessel each cell expressing a carrier mediated transport protein and different cells having different distinguishable characteristics. For example, Swanson et al. disclose both protein storage and lysosome-like secondary vacuoles, which can be considered a population of cells or, alternatively, the population of cells is differentiated by the addition of different hormones (e.g., see figure 3 showing hormone treatments), antigenicity (e.g., see figure 2), inhibitor treatment (e.g., see figure 5), dynamic (e.g., see figure 6), morphology/size and staining (see figures, 1 and 4; see also page 686, column 2, last paragraph). Swanson et al. further disclose (c) contacting the plurality of different cells with a plurality of complexes from the library simultaneously whereby at least one complex is bound to or internalized within one of the cells (e.g., see figure 4 showing

simultaneous contacting with both the CH₂Cl and CH₂SG and said CH₂SG is internalized within the cell). Swanson et al. also disclose **(d)** detecting a signal from the reporter of the at least one complex bound to or internalized within the cell in step (c) (e.g., see figures showing uptake of various conjugates; see especially figure 4 showing preferential generation of signal for proteolytically cleaved ZFR-CMAC-GS; see also discussion with regard to ZFR-GMAC-GS and conclusion identifying this compound as a substrate for a glutathione conjugate transporter that is a member of the ABC superfamily e.g., see page 695, column 1, paragraph 1). Finally, Swanson et al. disclose **(e)** determining the identity of the cell in step (c) from its distinguishable characteristic (e.g., see page 695, column 1, paragraph 2, “we conclude that at least two kinds of ATP-dependent transporters are present in protein storage vacuoles. One of these is an organic anion transporter that can be inhibited by probenecid and transports BCECF. The other is a glutathione conjugate transporter that is not inhibited by probenecid and transports MCB-GS. Both transporters may belong to the superfamily of ABC transporters”; see also different staining patterns, morphology, inhibition, etc. as noted above for the figures).

Response

8. Applicant's arguments directed to the above 35 U.S.C. § 102 rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection might have been modified from its original version to more clearly address applicants' newly amended and/or

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added claims and/or arguments.

Applicants argue, “Swanson et al. do not disclose a library of complexes, and do not disclose contacting the cells with a plurality off complexes from the library simultaneously” (e.g., see 8/20/07 Response, top of second to last page).

The Examiner respectfully disagrees. Swanson et al. disclose simultaneously contacting the cells with the CH₂Cl and CH₂SG compounds as set forth in figure 4 of Swanson et al. and noted in the rejection above.

Accordingly, the 35 U.S.C. § 102 rejection cited above is hereby maintained.

New Rejections

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claim 140, 141 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. For **claim 140**, use of the word “type” in the phrase “carrier-type” is vague and indefinite (e.g., see step (a)). The addition of the word “type” to an otherwise definite expression extends the scope of the expression so as to render it indefinite. See *Ex parte*

Copenhaver, 109 USPQ 118 (Bd. App. 1955). See also MPEP § 2173.05(b). The Examiner recommends “carrier-mediated transport protein” as a replacement” (e.g., compare to claims 1, 69, etc. that were just amended to remove this language). Therefore, claims 140 and all dependent claims are rejected under 35 U.S.C. § 112, second paragraph.

B. **Claim 141** recites the limitation "the population of cells" in the second to last line. There is insufficient antecedent basis for this limitation in the claim. Therefore, claim 141 and all dependent claims are rejected under 35 USC 112, second paragraph.

Allowable Subject Matter

10. Claims 69, 70, 72, 76, 77, and 142 are allowed. The following is a statement of reasons for the indication of allowable subject matter: The prior art of record does not teach or fairly suggest Applicants' claimed methods. The closest prior art of record, Homolya et al. and/or Swanson et al., do not teach the claimed compound/fluorophore/quencher moiety. The “AM” portions of fluorophores like BCECF-AM, Fura-2, Quin-2, etc. (e.g., see Homolya et al., figure 2) do not fall within the scope of the compound/fluorophore/quencher moiety because the fluorophore must be linked to the quencher via a linker (e.g., see independent claims 1 and 69), which is not the case for these molecules. That is, the potential “quencher” (i.e., the AM portion of each molecule) is attached directly to the fluorophore without the use of a linker. Furthermore, even if, *assuming arguendo*, the “first part” of the AM that is directly attached to the fluorophore (e.g., the cleavable ester) could be considered a linker; this part would still play a role as a quencher (e.g., blocking the ability of a heteroatom to donate electrons to a ring system)

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and thus would still need to be attached to the fluorophore via “another linker” that does not quench the fluorophore because, as mentioned above, a quencher cannot be directly attached to the fluorophore (including a quencher that also acts as a linker). This is consistent with Applicants’ specification that provides examples like acylated coumarins that function as “quenched” fluorophores (e.g., see page 35, lines 21-25). These acylated coumarins fall outside the scope of the current claims, just as the “AM” compounds do, because they do not possess anything (i.e., a linker) between the quencher and the fluorophore. Likewise, the Swanson et al. reference fails for the same reasons. Furthermore, the Swanson et al. and Homolya et al. references do not teach the simultaneous addition of compounds for screening. Swanson et al. and Homolya et al. also fail to teach the use of a reporter that promotes transcription of a promoter within a cell resulting in the expression of an enzyme.

Conclusion

Applicant's amendment necessitated any new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner’s supervisor, James (Doug) Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Jon D. Epperson/
Primary Examiner, AU 1639